

**REMARKS**

Reconsideration of this application is respectfully requested.

Claims 72-89 are pending in the application. Claims 72 and 80 have been amended. The amendments find support throughout the specification, for example, on page 38, ¶2, page 40, ¶1; pages 42-43, bridging ¶; page 45, ¶2; and pages 53-55. The amendments add no new matter.

**Rejection under 35 U.S.C. § 112, second paragraph**

Claims 72-89 were rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter, which applicants regard as the invention. The Office contends that the recitation of "hybridization conditions of Tm-42°C, Tm-20°C, and Tm-3°C" is vague and confusing.

Applicants traverse the rejection. Applicants submit that the skilled artisan recognizes that Tm-42°C, Tm-20°C, and Tm-3°C refer to hybridization conditions relative to the melting temperature of the duplex molecule. Applicants submit that this recitation is not vague and confusing, and submit Beltz et al., *Meth. Enzymol.* 100:266-285, 1983 (Exhibit 1), and Hyman et al., *J. Mol. Biol.* 77:189-196, 1973 (Exhibit 2), in support of the use of this terminology by the skilled artisan. Throughout these references, conditions are referred to with respect to the Tm of the duplex molecule.

For example, on page 271, ¶4, Beltz et al. states "In an aqueous solution at an incubation temperature of  $T_m-25^\circ$  . . . ." Figure 1, page 269, further illustrates the usage of temperature below  $T_m$  as a measurement for hybridization conditions. In Hyman et al., page 192, the recitations  $T_m-39^\circ\text{C}$ ,  $T_m-28^\circ\text{C}$ ,  $T_m-17^\circ\text{C}$ , and  $T_m-6^\circ\text{C}$  are used. Applicants submit that these references attest that the skilled artisan would understand the recitations of "hybridization conditions of  $T_m-42^\circ\text{C}$ ,  $T_m-20^\circ\text{C}$  and  $T_m-3^\circ\text{C}$ ".

The Office further contends that factors such as monovalent cation concentration, base composition, length of the duplex molecule, and concentration of formamide can alter the stringency of the hybridization conditions. Although applicants agree that these factors can be altered to affect the stringency of hybridization, applicants submit that these factors are all incorporated into the recitation of hybridization conditions with respect to  $T_m$ . As illustrated on page 272 of Beltz et al., second ¶,  $T_m$  can be calculated using equations, such as  $T_m=81.5 + 0.41 (G+C) +16.6 \log(\text{Na}^+) - 0.63(\% \text{ formamide}) - [300 + 2000(\text{Na}^+)]/d$ . Such an equation incorporates all of the parameters listed by the Office. For example, the effect of salt concentration or formamide concentration on the  $T_m$  can readily be calculated using such an equation. Therefore, the skilled artisan recognizes that hybridization conditions with respect to  $T_m$  can be varied in a predictable manner, for example, by adjusting the salt concentration

or formamide concentration. Accordingly, applicants respectfully submit that this recitation cannot be considered vague and confusing.

Solely to expedite prosecution of the application, applicants have amended claims 72 and 80 to point out that the hybridization conditions are with respect to the temperature below the melting temperature of the duplex molecule. Accordingly, applicants respectfully request withdrawal of the rejection.

The Office further contends that it is not readily manifest how the skilled artisan could measure the recited properties absent a description of the specific parameters involved in making any comparisons. Applicants disagree.

Applicants submit that the skilled artisan recognizes that quantitative comparisons of hybridization efficiency can be made simply by comparison of the signal produced by hybridization of the probe to the recited nucleic acid molecules. However, solely to expedite prosecution of the application, applicants have amended claim 72 and 80 to delete this recitation and to recite "an HIV-2 specific probe", as recommended by the Office as a means for obviating the rejection. Accordingly, applicants respectfully request withdrawal of the rejection.

**Rejection under 35 U.S.C. § 112, first paragraph**

Claims 72-89 were rejected under 35 U.S.C. § 112, first paragraph, because the specification allegedly does not reasonably enable one skilled in the art to make and/or use the invention commensurate in scope with the claims. The Office contends that the

claims are directed towards any nucleic acid capable of hybridizing to HIV-2 genomic RNA or DNA, and that the specification does not provide an adequate written description of those nucleotide probes that can be expected to function in the recited manner. The Office concludes that it would require undue experimentation for the skilled artisan to practice the claimed invention.

Applicants have amended claims 72 and 80 to recite that the claimed **methods** utilize an HIV-2 specific probe, which is an HIV-2 nucleic acid molecule that hybridizes to HIV-2ROD genomic DNA under specified hybridization conditions. Applicants submit that the claimed **methods** are fully enabled by the specification. The Federal Circuit has stated the test for the enablement requirement of 35 U.S.C. § 112, first paragraph:

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation.

Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986). Applicants submit that the skilled artisan could make and use the claimed invention without undue experimentation.

For example, using the teachings of the specification, the skilled artisan could use HIV-2ROD cDNA and restriction fragments, as taught by the specification on pages 25-26, to produce HIV-2 specific probes and to detect HIV-2 nucleic acid, for example, as taught in "Example III" on pages 36-38 of the specification. Similarly, HIV-2ROD gag

and *env* sequences, taught on pages 56-61 of the specification, could be used to produce HIV-2 specific probes and to detect HIV-2 nucleic acid.

Furthermore, applicants teach detailed methods for the isolation, propagation, cloning, preparation, and use of HIV-2 specific probes to detect HIV-2 nucleic acids. The specification teaches that HIV-2 was isolated from 11/12 patients from which it was attempted. (Specification at 42.) All 11 isolates were identified as HIV-2 by hybridization analysis using an HIV-2 specific probe. (Id.) Applicants submit that the skilled artisan, using the teachings of the specification, could prepare HIV-2 specific probes from any HIV-2 isolate without undue experimentation, and would expect that these probes could be used in the claimed **methods**, absent evidence to the contrary.

Applicants have disclosed embodiments that enable the use of the claimed **methods**. The skilled artisan recognizes that the claimed methods can be used to produce HIV-2 specific probes and to detect HIV-2 nucleic acid, absent evidence to the contrary. Applicants submit that the claimed methods are broadly applicable, and that no undue experimentation is required in their use. Since the successful use of the methods is predictable, the embodiments of the specification provide broad enablement. Accordingly, applicants respectfully request withdrawal of the rejection.

Furthermore, applicants submit that the specification provides an adequate written description of the claimed **methods**. In order to determine the appropriate disclosure of an application, "the specification as a whole must be considered." In re Wright, 9 U.S.P.Q. 2d 1649, 1651 (Fed. Cir. 1989). Furthermore, there is no particular

way in which the disclosure must convey the required information to one skilled in the art. "When the original specification accomplishes that [conveyance], regardless of how it accomplishes it, the essential goal of the description requirement is realized." Id. Thus, one must peruse the full scope of the disclosure, the working examples, the stated objectives, and all of the embodiments in order to determine whether in some way the written description conveys the invention to one skilled in the art. When this is done for the full disclosure in this case, applicants' specification meets the written description requirement of 35 U.S.C. § 112, first paragraph. As the specification states:

The invention naturally also relates to the use of cDNAs or their fragments (or recombinants containing them) as probes for the diagnosis of the presence or absence of HIV-2 virus in samples. . . The probes employed in this method for diagnosis of HIV-2 virus and in the diagnostic kits are in no way limited to the probes described above. They comprise, on the contrary, all the nucleotide sequences originating from the genome of the HIV-2 virus, of a variant of HIV-2 or of a structurally related virus . . .

(Specification at 53, ¶¶2-¶3.) Accordingly, applicants submit that the specification meets the requirements of 35 U.S.C. § 112.

Furthermore, applicants are not required to disclose every species encompassed by their claims, even in an unpredictable art. In re Angstadt, 537 F.2d 498, 502, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976). Rather, applicants can meet the sufficiency of disclosure through illustrative examples by teaching the skilled artisan to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility. In re Vaeck, 947 F.2d 488, 496, 20 U.S.P.Q. 2d 1438, 1445 (Fed. Cir. 1991). Applicants have provided detailed methods

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for determining which probes can function in the claimed **methods**. Therefore, applicants submit that only routine experimentation would be required to practice the claimed **methods**. Accordingly, applicants submit that the claims are enabled with respect to the requirements of 35 U.S.C. § 112, and respectfully request withdrawal of the rejection.

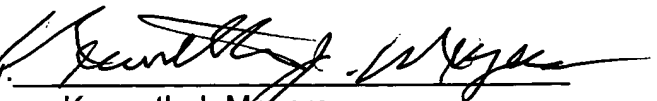
Applicants respectfully submit that this application is now in condition for allowance. If the Examiner should disagree, he is invited to contact the undersigned to discuss any remaining issues.

If there are any other fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 06-0916. If a fee is required for an extension of time under 37 C.F.R. § 1.136, not accounted for above, such an extension is requested, and the fee should also be charged to our Deposit Account.

Respectfully submitted,

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By:   
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